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INTERACTION OF FLUORIDE COMPLEXES DERIVED FROM GLASS-IONOMER CEMENTS WITH HYDROXYAPATITE

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A study has been undertaken of the interaction of complexed fluoride extracted from glass-ionomer dental cements with synthetic hydroxyapatite powder. Extracts were prepared from two commercial glass-ionomers (Fuji IX and ChemFlex) under both neutral and acidic conditions. They were analysed by ICP-OES and by fluoride-ion selective electrode with and without added TISAB to decomplex the fluoride. The pH of the acid extracts was 4, conditions under which fluoride complexes with protons as HF or HF₂⁻; it also complexes with aluminium, which was found to be present in higher amounts in the acid extracts. Fluoride was found to be almost completely complexed in acid extracts, but not in neutral extracts, which contained free fluoride ions.

Exposure of these extracts to synthetic hydroxyapatite powder showed that fluoride was taken up rapidly (within 5 minutes), whether or not it was complexed. SEM (EDAX) study of recovered hydroxyapatite showed only minute traces of aluminium taken up under all conditions. This showed that aluminium interacts hardly at all with hydroxyapatite, and hence is probably not involved in the remineralisation process.

INTRODUCTION

Glass-ionomer cements are widely used in clinical dentistry, with applications ranging from liners and bases to fissure sealants and full restorations [1, 2]. They are fabricated from complex ion-leachable glasses and aqueous solutions of water-soluble polymers, typically either poly(acrylic acid) or acrylic/maleic acid copolymer [3]. As such, they contain numerous ions, and a variety of ion-exchange processes underpin their uses [4].

One clinical advantage is their ability to release fluoride [4, 5]. This can be sustained for some considerable time, up to five years in vitro [6], and possibly longer in vivo. This fluoride can be replaced when the glass-ionomer cement is exposed to aqueous solutions of fluoride, for example fluoridated drinking water or following the use of fluoridated toothpaste [7, 8]. Recent studies have shown that this ability to take up fluoride declines as cements mature [9], and also that most of the fluoride taken up remains in the cement when the concentration of fluoride surrounding the cement falls, and is not released again, at least not within 24 hours [9].

Other ionic processes occur with these cements. For example, over time there is an exchange of ions at the interface with the tooth [10, 11]. This results in a strong,

lasting interfacial zone that enhances the adhesion of the cement to the tooth, and contributes to the long term retention of glass-ionomer restorations.

Fluoride is not the only ionic species to be released by these cements. Studies have shown that Na, Al, P and Si are also released in neutral conditions [12, 13], either as free positively charged ions or as negatively charged oxy-ions (e.g. PO₄³⁻). Ca²⁺ ions are also released under acidic conditions [12, 13]. Release of all ions is greater under acidic conditions than neutral ones, and is associated with a buffering effect [12], i.e. the pH of the surrounding acid is reduced by the cement in the process that leads to release of these ions. Similar behaviour has been observed in resin-modified glass-ionomers [14, 15]. They also release ions (Na, Al, Si, P, plus Ca in acidic conditions), with greater release into acid, with an associated buffering effect in the latter case [14].

The enhanced ion release in acid has been suggested as a clinical advantage [13]. This is because, in the presence of active caries, which typically has a pH of about 4.9 [16], greater amounts of fluoride ion are released from glass-ionomers, and this may have a preventive effect on the decay process in teeth. However, this low pH is also associated with release of substantial levels of aluminium, and aluminium is able to form a variety

of stable complexes with fluoride, for example AlF_4^- [17]. In addition, there is the possibility of the formation of complexes such as HF_2^- and also HF under acidic conditions below pH 5 [18]. Experimental results using a fluoride-ion selective electrode have demonstrated that, under acidic conditions, most if not all of the fluoride released from glass-ionomer cements is bound in some sort of complex or complexes, either with aluminium or hydrogen [12].

This raises the question that, if fluoride is complexed with aluminium, how readily is it taken up by the hydroxyapatite mineral phase of the tooth? The answer will indicate whether, under acidic conditions, complexation of the fluoride with aluminium potentially reduces the degree of protection conferred by fluoride, or whether fluoride is equally effective regardless of its state of complexation on release from the cement.

The present study has been undertaken to answer these questions. Overall, it had the following objectives:

- To determine how the composition of the neutral and acidic extracts of two commercial glass-ionomer cements varied with the pH of the extraction liquid;
- To measure fluoride levels in all the extracts both with and without the addition of TISAB (Total Ionic Solubility Acid Buffer) in order to measure, respectively, the total fluoride and the free fluoride present;
- To show how the free fluoride composition of the extracts changed when they were exposed to synthetic hydroxyapatite;
- To study the elemental composition of both the as-received and the recovered hydroxyapatite exposed to acidic extracts to show whether or not aluminium was present, and hence to establish whether aluminium was taken up by the hydroxyapatite powder.

EXPERIMENTAL

Two restorative grade glass-ionomer cements were employed, namely Fuji IX (capsulated, GC, Japan) and ChemFlex (Dentsply, Germany). Fuji IX was mixed on a vibratory dental mixer (Kent Dental, UK), with a 10 s mixing time. ChemFlex was hand-mixed and prepared on a glass block by spatulation of the components in the ratio of 0.74 : 0.1 powder:liquid by mass, as recommended by the manufacturers. In each case, freshly mixed cement pastes were placed between glass microscope slides and flattened, then cured in an incubator at 37°C for 1 hour. They were then crushed to a coarse powder using a pestle and mortar. Sufficient powdered cement was prepared from both materials to allow extraction with either deionised water or lactic acid (Analar grade, VWR, UK; concentration 20 mmol·dm⁻³, pH 2.7) in the ratio 0.5 g of powder to 25 cm³ of liquid. Extraction time was 1 hour, after which the powdered cement was separated from

the aqueous phase by filtration, and the aqueous phase retained. This was repeated several times to give sufficient quantities of each extract.

Fluoride levels (free and total) were determined for the initial extracts using a fluoride ion selective electrode (type 309/1050/03 combination electrode, ex BDH Poole, UK). For free fluoride, the electrode was simply dipped into the extract solution as prepared. For total fluoride, an equal volume of Total Ionic Solubility Acid Buffer, TISAB, (ex BDH, Poole, UK) was added to the extract to de-complex any bound fluoride, and a further determination made with the ion selective electrode. Values were corrected to take account of the effect of dilution with TISAB. Three determinations were made per extract, each on fresh volumes of solution.

Concentrations of other elements in solution were determined by ICP-OES using an Optima 4300 DV spectrometer (Perkin-Elmer, Santa Clara, California, USA) calibrated for each element that was determined (Si, P, Ca, Al, Sr). Elemental composition was measured for both water and lactic acid extracts for both cements. In addition, pH of all solutions was determined semi-quantitatively using 4-colour indicator strips (BDH, Poole, UK).

Following this, a series of experiments were carried out, each using 0.100 g of hydroxyapatite powder weighed into plastic centrifuge tubes, to which 5 cm³ of extract solution was added. Fluoride concentration (free and total) was then determined at 5, 10, 15 and 30 minutes, using the ion selective electrode. Each experiment was performed in triplicate, and mean values of free and total fluoride were determined, together with standard deviations. Differences were examined for significance using Student's t-test. A control experiment was also performed, in which fluoride solutions were placed in identical plastic tubes, and the concentration measured at regular time intervals up to 1 hour.

Separate exposures of hydroxyapatite powder to the lactic acid extracts were made over a 30 minute period, after which the powder was recovered from the solution by filtration and allowed to dry in air for 1 week at 37°C. These powders were then examined under the scanning electron microscope (JSM 5310LV Scanning Electron Microscope, JEOL, Japan) to determine elemental composition via the EDAX facility. An untreated sample of hydroxyapatite powder was also studied as a control. This was done with the specific aim of determining semi-quantitatively whether or not there had been any uptake of aluminium.

RESULTS

The initial compositions of the four extract solutions are shown in Tables 1 and 2. For both cements, extraction with neutral water led to the presence of both free and complexed fluoride, whereas extraction with

aqueous lactic acid gave only complexed fluoride, and no free fluoride was detected for either cement (Table 1). Total fluoride levels for Fuji IX were higher in acid, but did not differ significantly between water and lactic acid for ChemFlex. Both cements gave higher overall levels of ion release in lactic acid solution than in pure water (Table 2), with substantially more aluminium, calcium and strontium in lactic acid solution in each case. Values of pH recorded showed that the water was at or close to neutral, but that the lactic acid extracts were still substantially acidic (pH 4).

Table 1. Fluoride content (ppm) of extracts (Standard deviations in parentheses).

Cement	Water extract	Lactic acid extract
Fuji IX	Free F: 7.4 (2.5)	Free F: 0.0 (0.0)
	Total F: 16.9 (2.5)	Total F: 28.9 (6.5)
ChemFlex	Free F: 9.6 (4.3)	Free F: 0.0 (0.0)
	Total F: 21.4 (4.3)	Total F: 22.0 (3.2)

Table 2. Elemental composition (ppm) and pH of extracts (Standard deviations in parentheses).

Cement	Water extract	Lactic acid extract
Fuji IX	pH: 7	pH: 4
	Si: 4.05 (0.04)	Si: 21.32 (0.24)
	P: 0.58 (0.09)	P: 3.53 (0.05)
	Ca: 1.91 (0.01)	Ca: 3.38 (0.02)
	Al: 5.01 (0.05)	Al: 35.03 (0.41)
	Sr: 4.74 (0.09)	Sr: 52.43 (0.35)
ChemFlex	pH: 6	pH: 4
	Si: 7.79 (0.08)	Si: 35.93 (0.43)
	P: 1.90 (0.07)	P: 6.38 (0.07)
	Ca: 0.64 (0.01)	Ca: 7.92 (0.03)
	Al: 10.29 (0.23)	Al: 49.67 (0.52)
	Sr: 13.70 (0.34)	Sr: 95.94 (0.46)

The fluoride levels at various times following contact with hydroxyapatite powder for Fuji IX are shown in Table 3 and for ChemFlex are shown in Table 4. In each case, the behaviour was different in water and lactic acid solution. In water, there was a rapid drop in total fluoride concentration in the first five minutes, after which there remained reasonably steady and measurable levels of fluoride, most of which appeared to be free rather than complexed. The drop in free fluoride in the first five minutes was only slight.

By contrast, in lactic acid, there was only complexed fluoride present initially, and this had all disappeared by five minutes. After this, little or no fluoride could be detected.

The control experiment showed no changes in the level of fluoride measured, demonstrating that any reduction in fluoride in solution is due to its uptake by the hydroxyapatite, rather than the walls of the storage tubes.

Table 3. Measured fluoride content (ppm) for Fuji IX after exposure to hydroxyapatite powder (Standard deviations in parentheses).

Extract Time/min	Water		Lactic acid	
	Free	Total	Free	Total
0	7.4 (2.5)	16.9 (2.5)	0.00 (0.0)	28.9 (6.5)
5	6.9 (1.4)	2.9 (0.7)	0.0 (0.0)	0.0 (0.0)
10	6.3 (2.5)	1.8 (0.5)	0.0 (0.0)	0.0 (0.0)
15	5.6 (1.9)	2.3 (0.4)	0.0 (0.0)	0.0 (0.0)
30	5.5 (1.9)	1.6 (0.7)	0.0 (0.0)	0.0 (0.0)

Table 4. Measured fluoride content (ppm) for ChemFlex after exposure to hydroxyapatite powder (Standard deviations in parentheses).

Extract Time/min	Water		Lactic acid	
	Free	Total	Free	Total
0	9.6 (4.3)	21.4 (4.3)	0.00 (0.0)	22.0 (3.2)
5	8.0 (5.2)	2.6 (1.8)	0.0 (0.0)	0.6 (1.0)
10	5.8 (6.7)	3.4 (2.7)	0.0 (0.0)	1.7 (2.6)
15	6.3 (6.3)	2.4 (1.6)	0.0 (0.0)	0.2 (0.2)
30	6.0 (6.9)	2.3 (0.5)	0.0 (0.0)	0.3 (0.5)

Recovered samples of hydroxyapatite showed varying compositions, depending on the nature of the extract to which they had been exposed (Table 5). However, the main finding is that exposure to lactic acid extracts led to the uptake of only traces of aluminium.

Table 5. Composition of hydroxyapatite powder after exposure to lactic acid extracts of cement as determined by EDAX (element %).

Element	As-received HA	HA exposed to acid extract of ChemFlex	HA exposed to acid extract of Fuji IX
Ca	39.64	27.03	33.7
P	18.67	12.66	20.06
Al	0.18	0.25	0.45

DISCUSSION

Results for extraction studies showed that there were much higher levels of ion release in acidic conditions for all ions tested for both cements. In addition, there was no free fluoride, but rather, all appeared to be complexed. Results were inconsistent for free and total fluoride from Fuji IX in water, possibly because levels were low and near the limit of quantification of the ion selective electrode. Despite this, trends were clear, and the overall pattern of results suggested that fluoride was substantially free (uncomplexed) in neutral conditions, unlike the situation under acidic conditions.

The nature of the fluoride species present is not clear. As already mentioned, fluoride could complex to

either protons, as either HF or HF_2^- , or to aluminium. In all cases, this would result in fluoride being undetectable by the electrode. Such complexes are broken by the addition of TISAB, which is how the total fluoride can be determined.

Various aluminium species are known to occur in aqueous solution, including $\text{Al}(\text{H}_2\text{O})_6^{3+}$. This is a well characterised ion, with an octahedral AlO_6 core belonging to point group O_h [19]. Various aluminium-fluoride species have been proposed, including AlF_4^- , AlF_3 , AlF_2^+ and AlF^{2+} [20]. In addition, complexes of the type $\text{Al}(\text{OH})_m(\text{F})_n$ are known, including $\text{Al}(\text{OH})\text{F}_3^-$ and $\text{Al}(\text{OH})_2\text{F}$ [21]. The data obtained in the present study can be used to determine mole ratios of Al : F and these are shown in Table 6. It is not clear from these which of the possible aluminium-fluorine species are present in these solutions; possibly there is a complex series of equilibria between the various possibilities. What is clear is that the Al : F ratio decreases in acidic extraction conditions, i.e. the relative amount of fluoride ion increases.

Table 6. Aluminium:fluoride mole ratios in extracts.

Cement	Solution	Al:F ratio
Fuji IX	Water extract	1 : 0.37
	Acid extract	1 : 0.61
ChemFlex	Water extract	1 : 0.85
	Acid extract	1 : 1.59

When these solutions were exposed to hydroxyapatite, there was a rapid fall in the amount of fluoride in solution. This can be attributed to uptake of fluoride by the mineral phase, and is a well-established phenomenon [22]. Uptake appeared to go more readily and more-or-less to completion under acidic conditions, whereas measurable amounts of fluoride were still present after 30 minutes in neutral conditions. Under both conditions, though, there was a significant uptake of fluoride from solution.

Synthetic hydroxyapatite is known not to fully replicate the composition and structure of naturally occurring hydroxyapatite [23-25]. Natural hydroxyapatite is non-stoichiometric, with a high Ca : P ratio, and also contains between 3 and 8 % carbonate substitutions [24, 25]. These substitutions affect the chemical properties of the hydroxyapatite, reducing its crystallinity and increasing its solubility [23-26]. However, synthetic and natural hydroxyapatite are sufficiently similar to enable the synthetic version to be used as a model in *in vitro* experiments. The current synthetic hydroxyapatite had a Ca : P molar ratio of 1.65, which, though slightly less than the ideal stoichiometric ratio of 1.67, compares favourably with values of between 1.61 and 1.63 found in enamel and dentine [27].

Study of the recovered hydroxyapatite that had been exposed to acid extracts (i.e. the extracts which

contained the highest levels of aluminium) in the electron microscope using EDAX showed that there were extremely small differences in the measured aluminium levels of the samples. Comparison with the as-received hydroxyapatite showed there was an extremely small increase in aluminium levels but at such low levels that there had clearly been very little adsorption of aluminium by the mineral phase. This suggests that, unlike tin in stannous fluoride solution [28], there is almost no uptake of aluminium to accompany fluoride uptake by hydroxyapatite. This finding, together with the observation of the speed of fluoride depletion in the solutions, leads to the conclusion that complexation of fluoride with aluminium, or indeed, with protons, does not interfere with fluoride uptake. If anything, complexation enhances it. In the light of these findings, it seems likely that complexed fluoride produced in acidic solutions will interact with hydroxyapatite much as free fluoride does under neutral conditions, and thus will be effective in protecting the tooth against further demineralisation. We therefore confirm the conclusion of Forss [14] that the increased fluoride release in acidic conditions is clinically beneficial.

CONCLUSION

Under acidic extraction conditions, fluoride is released from glass-ionomer cements almost exclusively in complexed form, either with aluminium or with protons. By contrast, under neutral conditions, only a fraction of the fluoride is complexed, and the majority is free. Complexed fluoride from acidic solutions is able to be taken up rapidly by synthetic hydroxyapatite powder, much as it is under neutral conditions. Despite the presence of enhanced levels of aluminium in the acidic extracts, there were minimal increases in the level of this element in the surface of recovered hydroxyapatite powders, suggesting that aluminium interacts hardly at all with hydroxyapatite, and is therefore not involved in the remineralisation process.

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